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## SUSCEPTIBILITY TO HAY FEVER, AND ITS RELATION TO HEREDITY, AGE, AND SEASONS.

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### Susceptibility.

Hay fever is due to the protein of certain atmospheric pollens, the absorption of which causes the spasmodic vasomotor disturbances characteristic of this disease. As these pollens are inhaled by all persons within their potential radius but only about 1 per cent are affected, it is indicated that the persons affected suffer from an idiosyncrasy (allergy) which causes them to be sensitive to the effects of these pollens.

The susceptibility of hay-fever subjects varies within considerable limits, not only in their reaction to different pollens but also in the degree of this reaction.

The majority of hay-fever subjects in the Eastern and Southern States<sup>1</sup> are sensitive to the pollen of the ragweeds (fig. 1), and not to that of the grasses (fall hay fever). A smaller number is sensitive to the pollen of the grasses (fig. 2), but not to that of the ragweeds (spring hay fever). Others are sensitive to the pollens of both ragweeds and the grasses (spring-fall hay fever), while certain cases (8 per cent) are sensitive not only to these pollens but also to those of other plants and trees, so that they suffer from hay-fever attacks during the greater portion of the year (perennial form).

In addition to this difference in the character of the reaction, there is also a marked variation in its degree. Some patients, with a low susceptibility, suffer from hay fever only when the pollens are in great abundance in the air, so that they have only a few attacks during the season. Others, with a high susceptibility, suffer in various degrees during the whole of the pollinating season of the plants to whose pollens they are sensitive.

In order to place this relation of susceptibility to exposure on a practical basis, a formula has been devised representing the relative immunity to hay fever. In this the numerator is the resistance of the patient to the prevailing hay-fever pollens as determined by the intradermal diagnostic test, a completely negative test indicating the highest resistance and being represented by 100. The denominator is the highest average number of atmospheric pollens in the patient's locality per square centimeter of atmospheric-pollen plate for 24 hours,<sup>2</sup> the maximum average being represented by 100.<sup>3</sup>

<sup>1</sup> Hay-fever and Its Prevention. W. Scheppegrell, United States Public Health Reports, July 21, 1915 Reprint No. 349.

<sup>2</sup> The exposure of atmospheric-pollen plates gives a positive indication of the amount of pollen in the air, and therefore of the amount inhaled in its vicinity. We can always predict the hay-fever paroxysms by observing these records.

<sup>3</sup> Hay Fever and Hay-Fever Pollens, W. Scheppegrell, Archives of Internal Medicine, June, 1917.

The percentage below the resulting 1.00 indicates the patient's susceptibility to hay fever at that time.

If the resistance of the patient, for instance, is 50, and the highest average number of pollens per square centimeter is 50, then ( $50$  divided by  $50 = 1.00$ ) he is at the limit of his resistance to pollen sensitization, and any increase of exposure will cause an attack. When this is the case, his resistance usually becomes lower (anaphylaxis), as, for instance 35, so that for some time afterwards even 50 pollens per square centimeter ( $35$  divided by  $50 = 0.70$ , or — 30 per cent) will maintain an attack.<sup>1</sup>

Presuming that an absolute immunity were possible, which, as in the case of the infectious diseases, is still sub judice, the numerator becomes 100, and as the limit of the denominator is 100 ( $100$  divided by  $100$ ), then such a patient would be immune to any number of atmospheric pollens.

The diagnostic test is made by injecting into the skin of the forearm 5 units<sup>2</sup> of the pollen extract to be tested, this being 0.05 cubic centimeter of the strength of 100 units to the cubic centimeter. A positive reaction is indicated in 15 minutes by an urticarial wheal surrounded by an area of hyperemia, this reaction varying directly with the susceptibility of the patient and inversely as his resistance.

The records of the atmospheric-pollen plates (fig. 3) vary in different localities and seasons. The following table, from the records of the atmospheric-pollen plates at the laboratory of the American Hay-Fever-Prevention Association, shows the number of pollens per square centimeter and also indicates the effects of the wind, temperature, and rain, and the gradual disappearance of the ragweed (*Ambrosia*) pollens at the end of the hay-fever season:

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<sup>1</sup> Regarding the fractional method of expressing the relation of susceptibility to exposure, this was found necessary as explaining the apparently erratic occurrences of the attacks. The intradermal test in hay fever, as explained, gives a qualitative and quantitative indication of the susceptibility of the patient to pollen exposure, and is noted in clinical charts on a decimal basis as a guide for the doses in the immunizing treatment.

<sup>2</sup> The standard unit in pollen therapy is 0.001 milligram of pollen protein. This unit is not official. It was first suggested by Noon of London and is used by some manufacturers of pollen extracts in the United States.

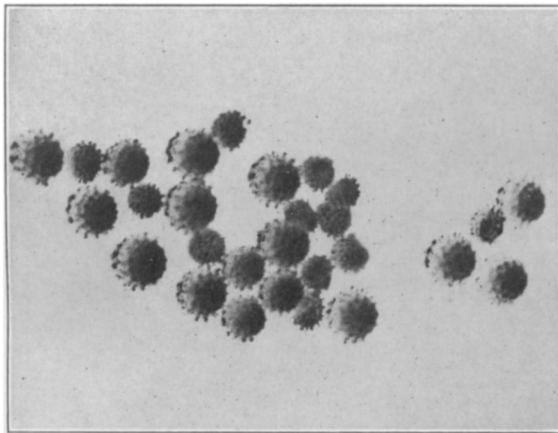


Fig. 1.—Pollen of common ragweed, *Ambrosia elatior*. (Reflected light.)

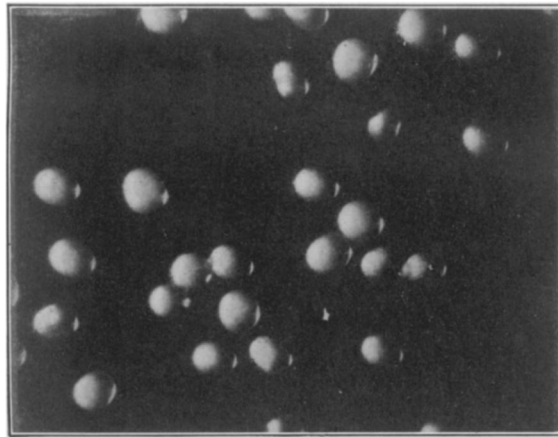


Fig. 2.—Pollen of Johnson grass, *Andropogon halepensis*. (Reflected light.)

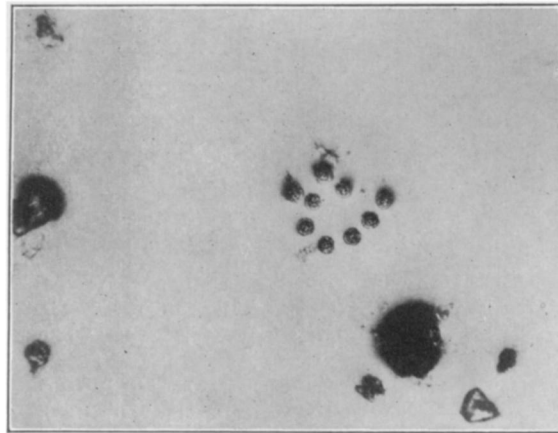


Fig. 3.—Atmospheric pollen plate, showing pollen of ragweed.

*Hay-fever pollens in relation to wind, temperature, and rain.*

	Number of grass pollens.	Number of ambrosia pollens.	Number of other pollens.	Number of pollen per square yard.	Maximum wind per hour.	Mean wind per hour.	Mean temperature.	Rain
					Miles.	Miles.	° F.	Inches.
Sept. 22.....	4	5	2	23	10	3.8	78	0.0
25.....		7		22	14	5.4	80	0.0
26.....	1	9		31	16	6.0	80	0.01
28.....		15		48	15	4.3	82	0.02
29.....		114		365	22	13.4	68	0.0
Oct. 1.....		36		115	16	7.5	68	0.0
2.....		19		61	14	7.4	71	0.0
3.....		6		19	12	5.9	72	0.0
4.....		7		22	12	6.2	74	0.0
5.....		11		35	21	10.7	73	0.01
6.....	2	6	2	29	16	7.2	78	0.01
7.....	1	7		26	17	7.9	76	0.02
8.....		2		6	12	4.3	80	1.85
9.....		8		26	7	2.9	80	0.0
10.....		12	1	42	18	9.6	74	0.0
11.....		11		35	18	7.7	73	0.0
13.....		3	1	13	7	4.3	77	0.0
14.....		9	2	35	10	5.0	78	0.0
17.....				0	25	14.0	72	2.58
18.....		1	4	16	24	11.5	74	0.19
19.....		23	5	90	15	7.9	76	0.0
20.....		5	5	32	23	13.4	62	0.0
21.....		12	2	45	15	8.5	58	0.0
24.....			2	6	8	4.2	67	0.0
25.....		1	1	6	15	7.1	70	0.0
26.....		8	2	32	17	10.1	62	0.0
27.....		1	3	13	15	8.5	66	0.0
28.....		1	8	29	12	6.5	67	0.0
29.....			1	3	9	4.5	70	0.0
31.....			2	6	8	3.7	72	0.0

From September 22 to 28 only patients with a low degree of relative immunity suffered from hay fever. On September 29, however, when the atmospheric pollen reached the maximum, all hay-fever subjects suffered severe paroxysms. After this date patients with a low degree of relative immunity suffered to some extent until October 26, when the fall hay fever ended on account of the disappearance of the ragweed pollens.

**Influence of Heredity.**

In order to determine the influence of heredity on hay fever, an analysis has been made of a series of 415 cases treated in the hay-fever clinic of the Charity Hospital at New Orleans and in private practice. This shows that over one-third of the cases (36.5 per cent) had relatives of the first degree (father, mother, sister, or brother) who suffered from hay fever.

The influence of heredity, however, is probably greater than this, as specific susceptibility may exist indefinitely without developing hay fever by reason of insufficient exposure to the hay-fever pollens. In order to understand this more clearly, we must consider the question of immunity to hay fever. The fact that 26 per cent of the cases of this series developed hay fever as late as from 30 to 40 years, and 8 per cent between 40 and 50 years, would indicate that immunity is relative at least in many cases.<sup>1</sup>

<sup>1</sup> The fact that many individuals pass through life without an attack of hay fever, although exposed to hay-fever pollens, indicates that immunity is absolute in some cases.

The development of hay fever at an advanced age is due to the fact that one attack of hay fever lowers the relative immunity of the patient to hay fever not only for an indefinite period but probably also, unless artificially raised, for the remainder of his life.

This is illustrated by the following case, which is not unusual in the records: This patient had lived in Louisiana for 42 years without developing hay fever, although his brother suffered from this disease. Fifteen years ago he spent a summer in western North Carolina and developed hay fever. He returned to Louisiana, but has continued to have hay fever every fall since this visit.

Pollenometric records<sup>1</sup> show that there is almost twice as much atmospheric ragweed pollen in western North Carolina as in Louisiana during the month of September. Assuming that this patient's relative immunity was 75 per cent, this was not sufficient to resist the exposure to the large amount of pollen inhaled during his visit to North Carolina. This attack, however, lowered his resistance so that he was no longer able to resist the exposure to the atmospheric ragweed pollen in Louisiana.

It is not necessary to travel any considerable distances to lower the relative immunity as in this instance. One patient, a woman of 40, lived for one season in a suburb of New Orleans where there was a large quantity of wild grass, and developed hay fever of the grass-pollen form. The following year she moved back to the central portion of the city, where formerly she had been immune to hay fever, but continued to have attacks for several seasons. In this case also the patient's relative immunity had been lowered by the first season's attacks resulting from greater exposure to the grass pollens.

#### **Proportion of Early and Autumnal Hay Fever.**

The proportion of the spring and autumnal hay-fever cases in this series was 6 and 44 per cent, respectively, but the number of cases of the combined form (spring-autumn) was unexpectedly high, being 42 per cent, or almost as high as the simple autumnal form. This differs materially from the previously published reports on this subject. In many of these cases the early hay fever is of only two or three weeks' duration, and is so much milder than the fall variety that many patients do not refer to it except on being closely questioned. The perennial form of hay fever, in which the paroxysms may develop at any season of the year, showing a susceptibility to many forms of hay-fever pollens, was also higher than was anticipated, being 8 per cent of all cases.

A noteworthy feature observed in the combined form of hay fever is that many patients commenced with the fall hay fever, and, after

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<sup>1</sup> Hay Fever and Hay-fever Pollens, W. Scheppegegrell, *Archives of Internal Medicine*, June, 1917.

two or more years, gradually also acquired the spring form. This indicates that hypersensitiveness to one form of pollen predisposes to hypersensitiveness to other pollens.

The proportion of the various forms of hay fever corresponded with the diagnostic test made in these cases. This test consists in the intradermal injection of 5 units of a pollen extract (100 units to the cubic centimeter) into the arm of the patient. Formerly this test was made by scarifying the skin and applying the pollen extract, but this has been abandoned for the intradermal injection, which is not only more reliable, but enables the quantitative effect of the pollen to be noted.

The results of these tests were as follows:

Percentage of cases which gave a positive test for—

Grass pollen only.....	6
Ragweed pollen only.....	44
Both grass and ragweed pollen <sup>1</sup> .....	50

A number of these also reacted to the chenopodium class of pollens<sup>2</sup> (dock, amaranths, chenopodium, Russian thistle, water hemp, etc.), especially among the patients suffering from the combined spring-autumn and the perennial forms.

#### Relative Proportion of the Sexes in Hay Fever.

In the cases of this series, 48 per cent were male and 52 per cent female. In the questionnaire made in Louisiana by the United States Public Health Service in 1916,<sup>3</sup> it was shown that 63 per cent of the cases of hay fever were males and 37 per cent females. The discrepancy in these percentages is due to the fact that women usually have more leisure than men to have chronic diseases treated. This applies especially to the poor, as shown by the fact that the percentage of females was relatively higher in our hay-fever clinic than in the cases treated in private practice.

#### The Ages of Hay Fever Cases.

The ages of the hay fever patients in this series (415 cases) vary from 6 to 64 years, the general average being 34 years. The decades were distributed as follows:

Percentage of cases between the age of—

1 and 10 years.....	1
10 and 20 years.....	19
20 and 30 years.....	24
30 and 40 years.....	31
40 and 50 years.....	11
50 and 60 years.....	10
60 and 70 years.....	4

<sup>1</sup> Hay Fever and Its Prevention. W. Scheppegegrell, Public Health Reports, July 21, 1916; Reprint No. 349.

<sup>2</sup> Classification of Hay-Fever Pollens from a Biological Standpoint. W. Scheppegegrell, Boston Medical and Surgical Journal, July, 1917.

<sup>3</sup> Hay Fever in Louisiana. W. Scheppegegrell, New Orleans Medical and Surgical Journal, October, 1916.

### Age of Development of Hay Fever.

The age at which hay fever developed in these cases varied from 4 years (1 case) to 49 years, the average being 27 years. The ages were distributed as follows:

Percentage of cases which developed between the age of—

1 and 10 years.....	5
10 and 20 years.....	23
20 and 30 years.....	38
30 and 40 years.....	26
40 and 50 years.....	8

This indicates that the most common period for the development of hay fever is between the ages of 20 and 40 (64 per cent). It corresponds closely with a former report, based on the questionnaire of the United States Public Health Service in Louisiana, in which 62 per cent of the cases were found to be between the ages of 20 and 40 years.

### Duration of Hay Fever.

The duration of hay fever in these cases varied from 1 month to 36 years, the general average being 9.7 years. The duration is divided as follows:

Percentage of cases which lasted from—

1 to 5 years.....	44
5 to 10 years.....	26
10 to 20 years.....	18
20 to 30 years.....	8
30 to 40 years.....	4

The question of the development of a natural immunity from continued exposure to the specific pollens is hard to determine, as it is difficult to eliminate the question of decreased exposure. If a patient moves to a locality in which the pollen exposure is below his relative immunity, he will not suffer from hay fever. This may also happen without changing his residence by the reduction of the weed areas beyond the potential radius of these pollens.

A number of cases have been recorded in which immunity gradually developed without change of exposure. That the natural development of immunity is a slow process, however, is indicated by the records, which show that 30 per cent of the cases had suffered for over 10 years, 12 per cent over 20 years, and 4 per cent over 30 years.